REMARKS

Claims 2-3, 5-21, 23-30, 37, 118-120, and 122-125 are pending in the present application. Claims 126-134 have been added. Accordingly, Claims 2-3, 5-21, 23-30, 37, 118-120, and 122-134 will be pending upon entry of the present amendment.

Support for new claims 126, 128, 130 and 132 can be found, for example, in the specification as originally filed at least on page 18 (see e.g., line 8). Support for new claims 127, 129, 131, and 133 can be found, for example, in the specification as originally filed at least on page 16 (see e.g., line 8). Support for new claim 134 can be found, for example, in the claims as originally filed and in the specification as originally filed at least at page 16 (see e.g., line 8) and page 18 (see e.g., line 8). No new matter has been added.

Applicants respectfully acknowledge the withdrawal of the rejection of claims 2, 3, 5-8, 11, 14-16, 18, 19, 23-26, 30, 37, 122 and 123 under 35 U.S.C. § 102 (e) as being anticipated by Garsky and the rejection of claims 4-8, 11, 13-17, 19, 25, 26, 30, and 118 under 35 U.S.C. § 103 (a) as obvious over Trouet *et al.* in view of Veronese, Dalborg, Gaetner, and Inada.

Applicants would also like to thank the Examiner for the telephonic interview held with Applicants' attorneys on May 24, 2007, during which the following rejections were discussed.

Rejection of Claims 2, 3, 5-8, 11, 13-19, 23-26, 28-30, 37, 118- 120 and 122-125 under 35 U.S.C. § 103(a)

Claims 2, 3, 5-8, 11, 13-19, 23-26, 28-30, 37, 118-120 and 122-125 have been rejected under 35 U.S.C. § 103 (a) as being unpatentable over Trouet *et al.* (WO 96/05863) or Trouet *et al.* (U.S. Patent No. 5,962,216) (collectively hereinafter referred to as "Trouet *et al.*"), each in view of Li *et al.* (*J. Biol. Chem.* (1990) 235, 2638-2641), Holcenberg *et al.* (*J. Biol. Chem.* (1975), 250 (11) 4165-4170), Hall (U.S. 4,144,333), Guthiel (U.S. 5,574,107), or LaRochelle (U.S. 5,833,986). In particular, the Examiner asserts that succinylation of the positively charged prodrug, βAla-Leu-Ala-Leu-Dox, taught by Trouet *et al.*, would have been obvious in view of the secondary references which teach succinylation for the purposes of (1) increasing the half life of proteins (Li *et al.* and Holcenberg *et al.*) and (2) protecting amino groups from degradation (Gutheil and Hall).

Applicants respectfully traverse this rejection. In support of Applicants' position, Applicants submit herewith a declaration by Dr. Sanjeev Gangwar. As attested by Dr.

Gangwar, the foregoing references would not have made the presently claimed invention obvious, because the reasons for succinylating proteins taught by these references would not have applied to the prodrug peptides recited in the present claims, including βAla-Leu-Ala-Leu-Dox.

Specifically, one of ordinary skill in the art would not have been motivated to succinylate the βAla-Leu-Ala-Leu-Dox prodrug described by Trouet *et al.* to increase the prodrug's half-life and/or protect it from degradation, because Trouet *et al.* explicitly teach that the prodrugs "remain stable in the serum and in the blood, and [are] insensitive to the action of the circulating proteinases and peptidases associated with the red cells" (see e.g., U.S.5,962,216, col. 8, lines 41-44).

In fact, Trouet *et al.* teach that the use of a non-genetically encoded amino acid (i.e., an amino acid not present in mammals), such as β-alanine, alone is sufficient to stabilize such prodrugs and to prevent their degradation *in vivo.* Trouet *et al.* also teach that succinyl groups alone can be used as stabilizing groups. The authors do not teach or suggest the use of succinyl groups in combination with at least one non-genetically encoded amino acid, as presently claimed, for any purpose.

Similarly, although Holcenberg *et al.*, Li *et al.*, Gutheil, and Hall teach the use of succinylation to decrease the amount of degradation of proteins *in vivo,* one of ordinary skill in the art would not have been motivated to apply this use to the prodrugs recited in the present claims, because Trouet *et al.* taught that these prodrugs were already specifically designed to be stable in whole blood and selectively cleaved in the vicinity of particular target cells.

For at least the foregoing reasons, Applicants respectfully request that this rejection of claims 2, 3, 5-8, 11, 13-19, 23-26, 28-30, 37, 118-120 and 122-125 under 35 U.S.C. § 103(a) be withdrawn.

Rejection of Claims 2, 3, 5-8, 11, 13-19, 23-26, 28-30, 37, 118- 120 and 122-124 under Judicially Created Doctrine of Obviousness Type Double Patenting

Claims 2, 3, 5-8, 11, 13-19, 23-26, 28-30, 37, 118-120 and 122-124 are rejected under the judicially created doctrine of nonstatutory obviousness-type double patenting as being unpatentable over Trouet *et al.* (U.S. 5,962,216), in view of Li *et al.* (*J. Biol. Chem.* (1990) 235, 2638-2641), Holcenberg *et al.* (*J. Biol. Chem.* (1975), 250 (11) 4165-4170), Hall (U.S. 4,144,333), Gutheil (U.S. 5,574,107), or LaRochelle (U.S. 5,833,986).

Applicants respectfully traverse this rejection for at least the reasons provided above in relation to why the presently claimed invention is not obvious over Trouet *et al.* (U.S. 5,962,216), alone or in combination with the cited references. These reasons apply

equally to the claims of Trouet *et al.* Accordingly, Applicants respectfully request that this rejection be withdrawn.

Provisional Rejection of Claims 2, 3, 5-12, 14, 15, 17-19, 21, 23-27, 30, 37, and 122-124 under Judicially Created Doctrine of Obviousness Type Double Patenting

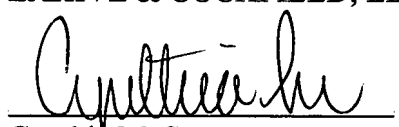
Claims 2, 3, 5-12, 14, 15, 17-19, 21, 23-27, 30, 37, and 122-124 are provisionally rejected under the judicially created doctrine of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-8, 11, 13-18, 23-29, 57, 58, 60, 61 and 63 of Pickford *et al.* (U.S.S.N. 10/311,411).

While in no way admitting that claims 2, 3, 5-12, 14, 15, 17-19, 21, 23-27, 30, 37, and 122-124 are obvious over claims 1, 4-8, 11, 13-18, 23-29, 57, 58, 60, 61 and 63 of U.S.S.N. 10/311,411, Applicants will consider submitting a terminal disclaimer in compliance with 37 C.F.R. §1.321(b) and (c), if appropriate, if and when both applications are allowed.

SUMMARY

It is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Respectfully submitted,
LAHIVE & COCKFIELD, LLP



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